Ethics and Evidence-Based Healthcare

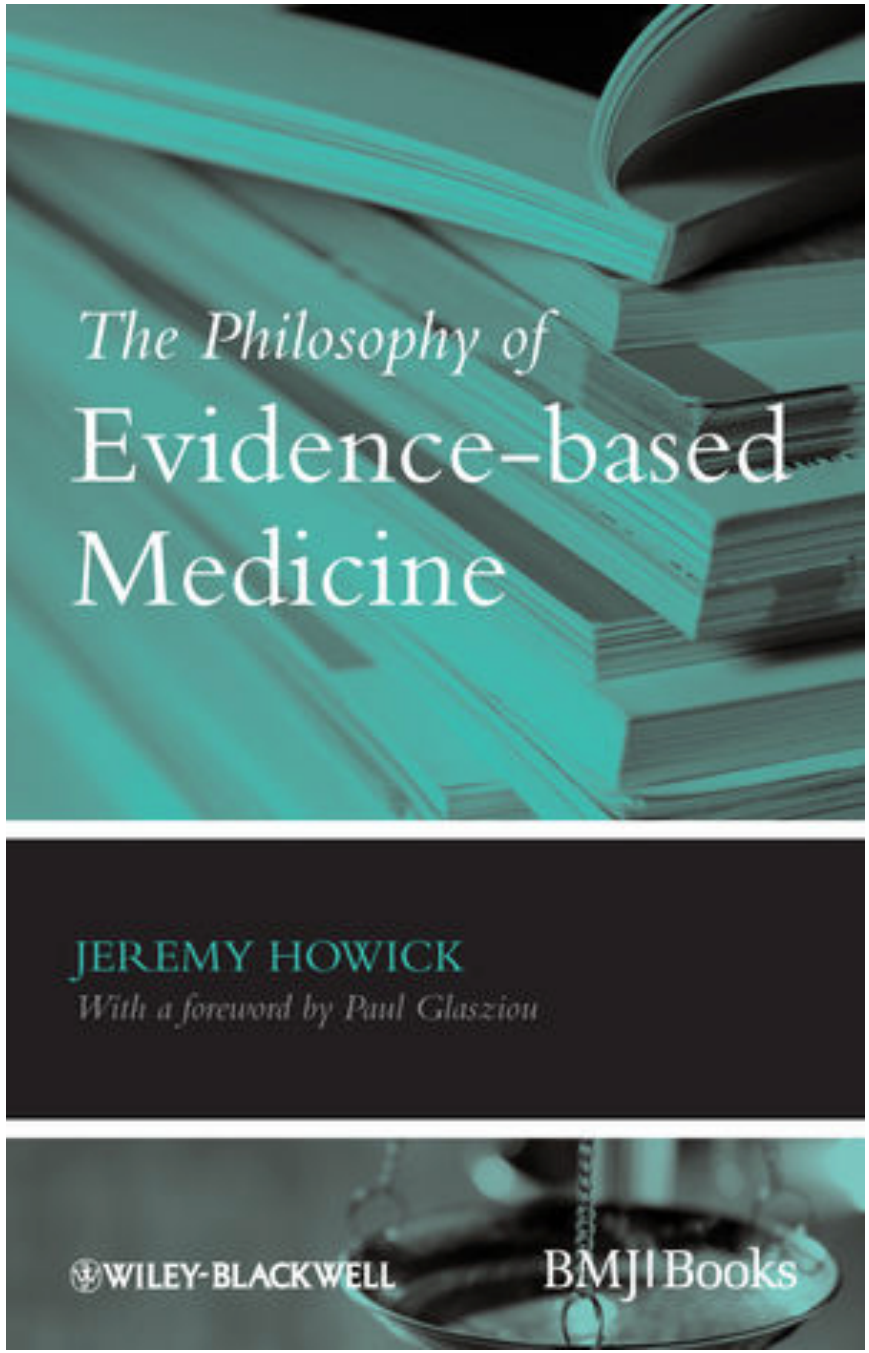
Jeremy Howick

Before you leave the room, you will

- … learn basic principles of medical ethics

- … apply the basics to construct your own arguments and critically appraise others

- … to "**think evidence, think ethics**", "**think ethics, think evidence**"


The Philosophy of
Evidence-based
Medicine
JEREMY HOWICK
With a foreword by Paul Glasziou
WILEY-BLACKWELL
BMJ Books

How do you verify the following:

1. “a blood transfusion will save the patient”

2. “you should force the Jehovah’s Witness to have a blood transfusion although they do not wish to have one”

What is ethics?

Descriptive versus normative claims

Descriptive

"randomized trials **do** rule out more bias than other types of evidence"

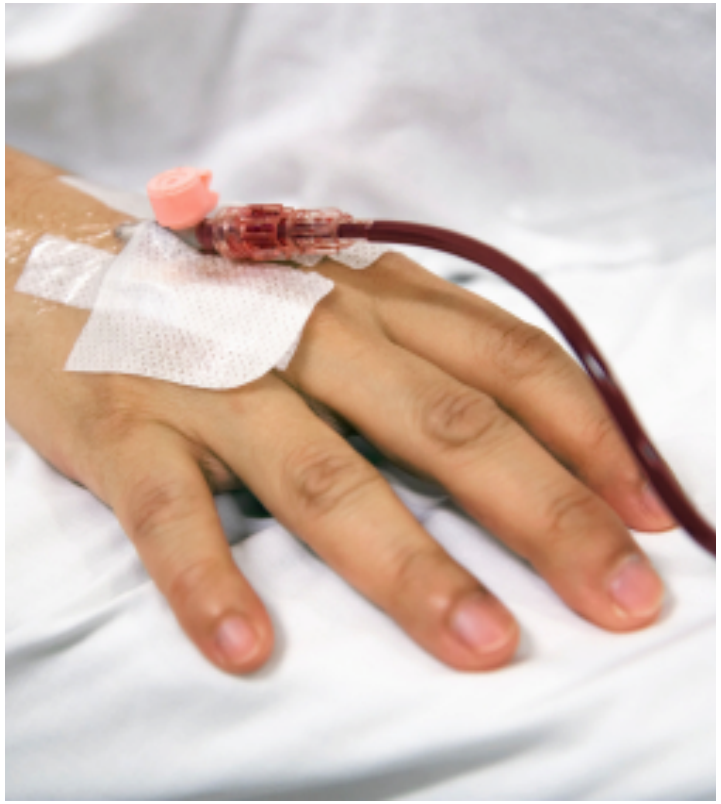
Normative

"you **should** base your decisions on randomized trials"

Transfusions **can** save your life, but what **should** you do?

What should a Jehovah's Witness do?

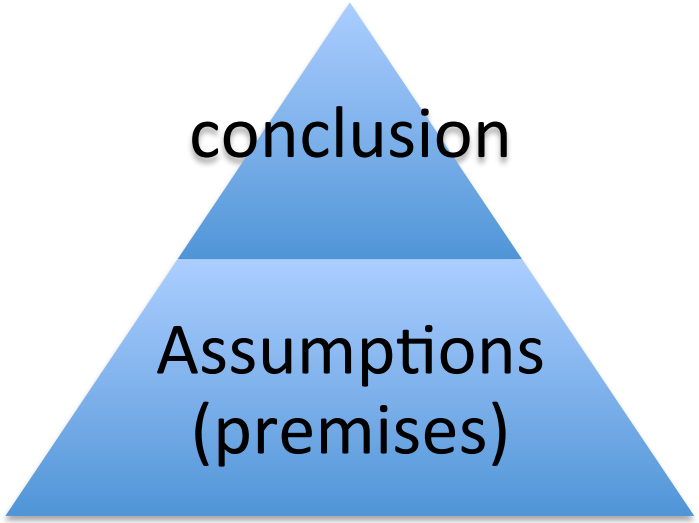
"Abstain from ... fornication and from what is strangled and from blood" *Acts 15:19-21*



Critical thinking = question the assumptions upon which the conclusion rests

1. State your position (1. conclusion)
2. State the we should believe your position (2. premises)

Critical thinking = question the assumptions upon which the conclusion rests (and the inference from the premises to the conclusion



?

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Is it ethical for experts to override evidence because their patients are special?

Computer-aided Diagnosis of Acute Abdominal Pain

F. T. de DOMBAL, D. J. LEAPER, J. R. STANILAND, A. P. McCANN, JANE C. HORROCKS

British Medical Journal, 1972, 2, 9-13

The computing system's overall diagnostic accuracy (91·8%) was significantly higher than that of the most senior member of the clinical team to see each case (79·6%). It is suggested as a result of these studies that the provision of such a system to aid the clinician is both feasible in a real-time clinical setting, and likely to be of practical value, albeit in a small percentage of cases.

Is it ethical to base decisions on observational studies?

Estrogen Replacement Therapy and Coronary Heart Disease: A Quantitative Assessment of the Epidemiologic Evidence[1,2]

MEIR J. STAMPFER, M.D.,*,†,[3] AND GRAHAM A. COLDITZ, M.D.*,‡

CONCLUSION

The preponderance of evidence from the epidemiologic studies strongly sup-
ports the
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Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women

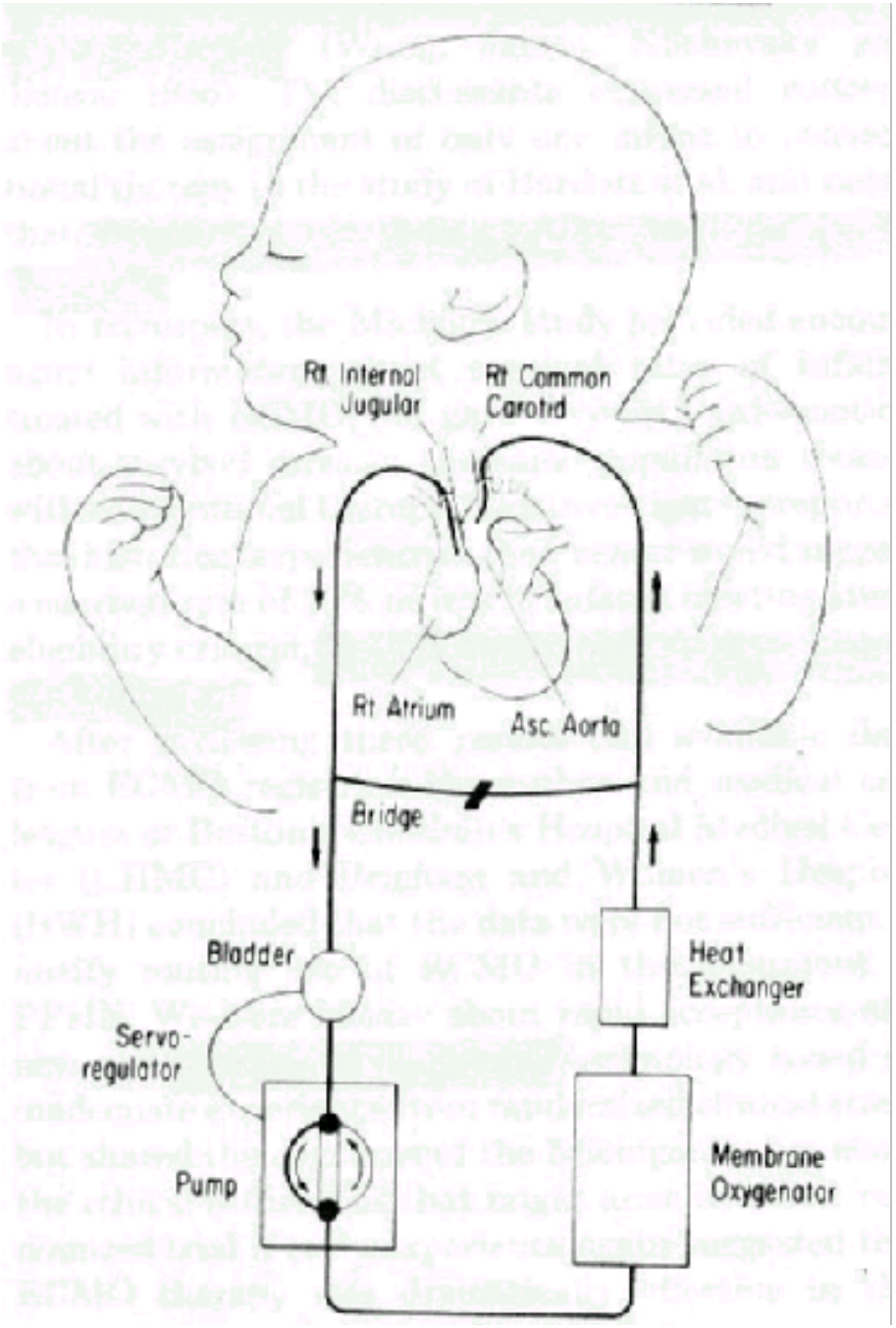
Principal Results From the Women's Health Initiative Randomized Controlled Trial

Conclusions Overall health risks exceeded benefits from use of combined estrogen plus progestin for an average 5.2-year follow-up among healthy postmenopausal US women. All-cause mortality was not affected during the trial. The risk-benefit profile found in this trial is not consistent with the requirements for a viable intervention for primary prevention of chronic diseases, and the results indicate that this regimen should not be initiated or continued for primary prevention of CHD.

JAMA. 2002;288:321-333 www.jama.com

The story of ECMO

- Extra-corporeal membraneous oxygenation.
- **With the new technique 80% of babies survived** (**with 'standard care', 80% died**).
- They "felt compelled to conduct a … randomized study".
- Yet they "anticipated that most …control patients would die"



The story of ECMO

First trial

- Protocol: “Randomized play the winner”
- Result: 11 babies assigned ECMO and lived
- 1 baby assigned standard treatment and died

Second trial

- Protocol: orthodox randomisation with $p<0.05$
- with stopping rule – stop after 4 deaths in either arm
- RESULT: 9 babies assigned to ECMO, all survived
- 10 babies assigned to standard treatment, 4 died

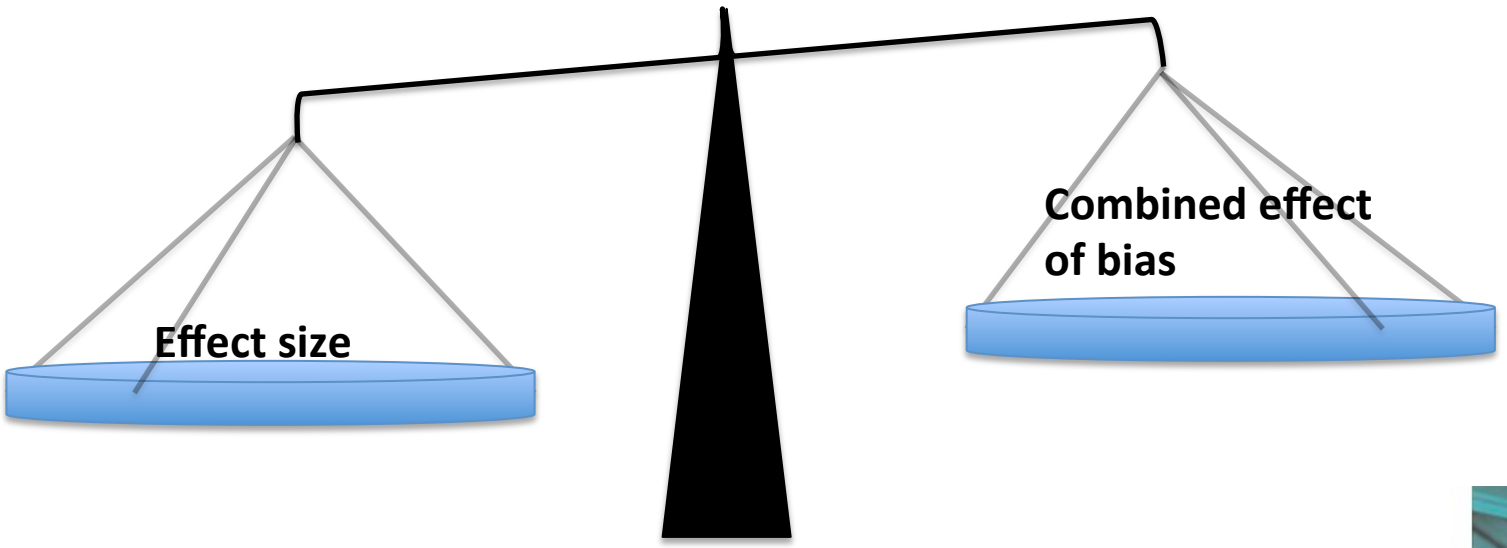
The story of ECMO

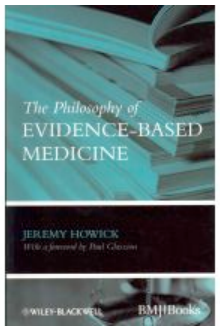
- (Pocock) ".. a decision was taken to halt randomization when the data disclosed four deaths among ten infants receiving conventional medical treatment compared with none among nine infants having ECMO (p= 0.054)…
- … However, with only 19 patients this does not represent strong evidence of the superiority of ECMO and provides little scope for making reliable judgments on the benefits of this treatment for universal use in such newborn infants in the future."
- Thus a ***third* trial** was recommended and performed.

Equipoise

- A physician may offer enrollment to a randomized trial only when there is ***equipoise***.
- Equipoise is (roughly) uncertainty about the relative benefits and harms of the treatment.

Resolving the issue of whether randomized trials are ethical: it depends on the evidence!





Recap

- If you don't base your decisions on **best evidence** you are acting **unethically**.
- One more example that is slightly more complicated…

Is it ethical to conduct 'placebo' controlled trials when there is an established therapy?

Clinician

Researcher

Background: PCTs and ACTs

- A ‘placebo’ controlled trial, or PCT, compares the experimental treatment with a ‘placebo’.

- An ‘active’ controlled trial, or ACT, compares the experimental treatment with an established treatment.

Statements about the superiority of PCTs

Declaration of Helsinki:

a placebo controlled trial may be ethically acceptable even if proven therapy is available, under the following circumstances:

- Where for **compelling and scientifically sound methodological reasons** *its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic, or therapeutic method* … (WMA 2001`, emphasis added).

Where are the reasons?

Reasons

1. ACTs do not provide evidence that the new intervention is superior to ‘placebo’.
2. ACTs do not provide a measure of ‘absolute effect size’.
3. ACTs require a larger sample size.

Target Article

Questioning the Methodologic Superiority of 'Placebo' Over 'Active' Controlled Trials

Jeremy Howick, University of Oxford

Consequently, the apparent tension between clinical and research ethics as far as the use of 'placebo' controls dissolves: methodological considerations do not support the use of PCTs where there is an established therapy. The ethical duty of the clinician to provide the best care (and avoid PCTs) where there is an established treatment available stands unchallenged by the moral duties of the clinical researcher to use the best method. The Declaration of Helsinki should retract the statement that PCTs can be justified on methodological grounds (where there is an available established therapy) and IRBs should dismiss claims that PCTs are methodologically superior to ACTs as grounds to approve PCTs where standard therapy is available.

Exercise

- Give an example of an ethical issue arising in your research or practice.
- Which of the four principles applies / can help you resolve the issue?

Next steps…

- MII, Research Ethics
- History and Philosophy of EBHC (www.conted.ox.ac.uk/B900-77)

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Thank you!

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